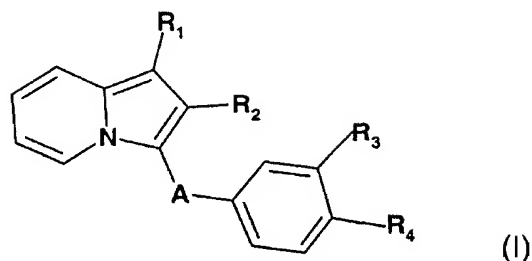


In the Claims

1. (Currently Amended) A compound of formula I,



in which

- **R<sub>1</sub>** represents a hydroxyl radical, a linear or branched alkoxy radical of 1 to 5 carbon atoms, a carboxyl radical, an alkoxycarbonyl radical of 2 to 6 carbon atoms or a radical of formula:

- -NR<sub>5</sub>R<sub>6</sub>
- -NH-SO<sub>2</sub>-Alk
- -NH-SO<sub>2</sub>-Ph
- -NH-CO-Ph
- -N(Alk)-CO-Ph
- -NH-CO-NH-Ph
- -NH-CO-Alk
- -NH-CO<sub>2</sub>-Alk
- -O-(CH<sub>2</sub>)<sub>n</sub>-cAlk
- -O-Alk-COOR<sub>7</sub>
- -O-Alk-O-R<sub>8</sub>
- -O-Alk-OH
- -O-Alk-C(NH<sub>2</sub>):NOH
- -O-Alk-NR<sub>5</sub>R<sub>6</sub>
- -O-Alk-CN
- -O-(CH<sub>2</sub>)<sub>n</sub>-Ph

- -O-Alk-CO-NR<sub>5</sub>R<sub>6</sub>
- -CO-NH-(CH<sub>2</sub>)<sub>m</sub>-COOR<sub>7</sub>
- -CO-NH-Alk

in which

- Alk represents an alkyl radical or a linear or branched alkylene radical of 1 to 5 carbon atoms,
- cAlk represents a cycloalkyl radical of 3 to 6 carbon atoms,
- n represents an integer from 0 to 5,
- m represents an integer from 1 to 5,
- R<sub>5</sub> and R<sub>6</sub>, which are identical or different, each represent a hydrogen atom, a linear or branched alkyl radical of 1 to 5 carbon atoms or a benzyl radical,
- R<sub>7</sub> represents a hydrogen atom or an alkyl radical of 1 to 5 carbon atoms,
- R<sub>8</sub> represents an alkyl radical of 1 to 5 carbon atoms or a radical -CO-Alk,
- Ph represents a phenyl radical which is optionally substituted with one or more halogen atoms, with one or more alkoxy radicals of 1 to 5 carbon atoms, with one or more carboxyl radicals or with one or more alkoxycarbonyl radicals of 2 to 6 carbon atoms,
- **R<sub>2</sub>** represents a hydrogen atom, an alkyl radical of 1 to 5 carbon atoms, a haloalkyl radical of 1 to 5 carbon atoms containing 3 to 5 halogen atoms, a cycloalkyl radical of 3 to 6 carbon atoms or a phenyl radical which is optionally substituted with one or more halogen atoms, with one or more alkoxy radicals of 1 to 5 carbon atoms, with one or more carboxyl radicals or with one or more alkoxycarbonyl radicals of 2 to 6 carbon atoms,
- **A** represents a radical -CO-, [[-SO- or -SO<sub>2</sub>-],]
- **R<sub>3</sub>** and **R<sub>4</sub>**, which are identical or different, each represent a hydrogen atom, an alkoxy radical of 1 to 5 carbon atoms, an amino radical, a carboxyl radical, an alkoxycarbonyl radical of 2 to 6 carbon atoms, a hydroxyl radical, a nitro radical, a hydroxyamino radical, a radical of formula
  - -Alk-COOR<sub>7</sub>

- -NR<sub>5</sub>R<sub>6</sub>
- -NH-Alk-COOR<sub>7</sub>
- -NH-COO-Alk
- -N(R<sub>11</sub>)-SO<sub>2</sub>-Alk-NR<sub>9</sub>R<sub>10</sub>
- -N(R<sub>11</sub>)-SO<sub>2</sub>-Alk
- -N(R<sub>11</sub>)-Alk-NR<sub>5</sub>R<sub>6</sub>
- -N(R<sub>11</sub>)-CO-Alk-NR<sub>9</sub>R<sub>10</sub>
- -N(R<sub>11</sub>)-CO-Alk
- -N(R<sub>11</sub>)-CO-CF<sub>3</sub>
- -NH-Alk-HetN
- -O-Alk-NR<sub>9</sub>R<sub>10</sub>
- -O-Alk-CO-NR<sub>5</sub>R<sub>6</sub>
- -O-Alk-HetN

in which n, m, Alk, R<sub>5</sub>, R<sub>6</sub> and R<sub>7</sub> have the meaning given above for R<sub>1</sub>, and

- R<sub>9</sub> and R<sub>10</sub>, which are identical or different, each represent a hydrogen atom or an alkyl radical of 1 to 5 carbon atoms,
- R<sub>11</sub> represents a hydrogen atom or a radical -Alk-COOR<sub>12</sub> where R<sub>12</sub> represents a hydrogen atom, an alkyl radical of 1 to 5 carbon atoms or a benzyl radical,
- HetN represents a 5- or 6-membered heterocycle containing at least one nitrogen atom and optionally another heteroatom chosen from nitrogen and oxygen,

or R<sub>3</sub> and R<sub>4</sub> form together a 5- to 6-membered unsaturated heterocycle,

or a pharmaceutically acceptable salt thereof,

provided, however, that when R<sub>3</sub> represents an alkoxy radical and R<sub>4</sub> represents a radical -O-Alk-NR<sub>9</sub>R<sub>10</sub> or a hydroxyl radical, R<sub>1</sub> does not represent an alkoxy radical, and provided that when R<sub>1</sub> is an alkoxycarbonyl radical, and R<sub>2</sub> is hydrogen or methyl, then at least one of R<sub>3</sub> and R<sub>4</sub> is other than hydrogen, and provided that the compound of formula I is other than [4-[3-(dibutylamino)propoxy]phenyl](2-ethyl-1-hydroxy-3-indolizinyI)methanone or a pharmaceutically acceptable salt thereof.

2. (Currently Amended) A compound according to Claim 1, in which

- $R_1$  represents a hydroxyl radical, a linear or branched alkoxy radical of 1 to 5 carbon atoms, a carboxyl radical, an alkoxycarbonyl radical of 2 to 6 carbon atoms or a radical of formula:
  - $-NR_5R_6$
  - $-NH-SO_2-Alk$
  - $-NH-SO_2-Ph$
  - $-NH-CO-Ph$
  - $-N(Alk)-CO-Ph$
  - $-NH-CO-NH-Ph$
  - $-NH-CO-Alk$
  - $-NH-CO_2-Alk$
  - $-O-(CH_2)_n-cAlk$
  - $-O-Alk-COOR_7$
  - $-O-Alk-O-R_8$
  - $-O-Alk-OH$
  - $-O-Alk-NR_5R_6$
  - $-O-Alk-CN$
  - $-O-(CH_2)_n-Ph$
  - $-O-Alk-CO-NR_5R_6$
  - $-CO-NH-(CH_2)_m-COOR_7$
  - $-CO-NH-Alk$

in which

- Alk represents an alkyl radical or a linear or branched alkylene radical of 1 to 5 carbon atoms,
- cAlk represents a cycloalkyl radical of 3 to 6 carbon atoms,
- n represents an integer from 0 to 5,
- m represents an integer from 1 to 5,

- $R_5$  and  $R_6$ , which are identical or different, each represent a hydrogen atom, a linear or branched alkyl radical of 1 to 5 carbon atoms or a benzyl radical,
  - $R_7$  represents a hydrogen atom or an alkyl radical of 1 to 5 carbon atoms,
  - $R_8$  represents an alkyl radical of 1 to 5 carbon atoms or a radical -CO-Alk,
  - Ph represents a phenyl radical which is optionally substituted with one or more halogen atoms, with one or more alkoxy radicals of 1 to 5 carbon atoms, with one or more carboxyl radicals or with one or more alkoxy carbonyl radicals of 2 to 6 carbon atoms,
- $R_2$  represents an alkyl radical of 1 to 5 carbon atoms, a trifluoromethyl radical, a cycloalkyl radical of 3 to 6 carbon atoms or a phenyl radical which is optionally substituted with one or more halogen atoms, with one or more alkoxy radicals of 1 to 5 carbon atoms, with one or more carboxyl radicals or with one or more alkoxy carbonyl radicals of 2 to 6 carbon atoms,
- A represents a radical -CO- [[or -SO<sub>2</sub>-]],
- $R_3$  and  $R_4$ , which are identical or different each represent a hydrogen atom, an alkoxy radical of 1 to 5 carbon atoms, an amino radical, a carboxyl radical, an alkoxy carbonyl radical of 2 to 6 carbon atoms, a nitro radical, a hydroxyamino radical, a radical of formula
- -Alk-COOR<sub>7</sub>
  - -NR<sub>5</sub>R<sub>6</sub>
  - -NH-Alk-COOR<sub>7</sub>
  - -NH-COO-Alk
  - -N(R<sub>11</sub>)-SO<sub>2</sub>-Alk-NR<sub>9</sub>R<sub>10</sub>
  - -N(R<sub>11</sub>)-SO<sub>2</sub>-Alk
  - -N(R<sub>11</sub>)-Alk-NR<sub>5</sub>R<sub>6</sub>
  - -N(R<sub>11</sub>)-CO-Alk-NR<sub>9</sub>R<sub>10</sub>
  - -N(R<sub>11</sub>)-CO-Alk
  - -N(R<sub>11</sub>)-CO-CF<sub>3</sub>
  - -NH-Alk-HetN
- in which n, m, Alk,  $R_5$ ,  $R_6$  and  $R_7$  have the meaning given above for  $R_1$ , and

- $R_9$  and  $R_{10}$ , which are identical or different, each represent a hydrogen atom or an alkyl radical of 1 to 5 carbon atoms,
- $R_{11}$  represents a hydrogen atom or a radical  $-Alk-COOR_{12}$  where  $R_{12}$  represents a hydrogen atom, an alkyl radical of 1 to 5 carbon atoms or a benzyl radical,
- HetN represents a 5- or 6-membered heterocycle containing at least one nitrogen atom and optionally another heteroatom chosen from nitrogen and oxygen.

3. (Previously presented) A compound according to Claim 2 wherein

- $R_1$  represents an alkoxy radical of 1 to 5 carbon atoms, a carboxyl radical, a radical  $-O-Alk-COOH$  in which Alk represents an alkylene radical of 1 to 5 carbon atoms, a radical of formula  $-O-Alk-Ph$  in which Alk represents an alkylene radical of 1 to 5 carbon atoms and Ph represents a phenyl radical which is optionally substituted with one or more halogen atoms or with one or more alkoxy radicals of 1 to 5 carbon atoms or with one or more carboxyl radicals, a radical of formula  $-NH-CO-Ph$ , a radical of formula  $-NH-SO_2-Ph$  or a radical of formula  $-NH-CO-NH-Ph$ ,
- $R_2$  represents an alkyl radical of 1 to 5 carbon atoms,
- A represents a radical  $-CO-$ , and
- $R_3$  and  $R_4$ , which are different, each represent a hydrogen atom, an alkoxy radical of 1 to 5 carbon atoms, an amino radical, a carboxyl radical or an alkoxycarbonyl radical of 2 to 6 carbon atoms.

4. (Previously presented) A compound according to Claim 1 selected from the group consisting of:

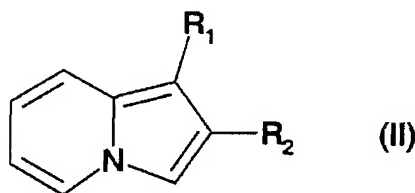
- (4-amino-3-methoxyphenyl)(1-methoxy-2-methylindolizin-3-yl)methanone,
- 3-(4-amino-3-methoxybenzoyl)-2-methylindolizin-1-yl carboxylic acid,
- 2-{[3-(4-amino-3-methoxybenzoyl)-2-methylindolizin-1-yl]oxy}acetic acid,
- (4-amino-3-methoxyphenyl){1-[(4-chlorobenzyl)oxy]-2-methylindolizin-3-yl}methanone,
- (4-amino-3-methoxyphenyl){1-[(3-methoxybenzyl)oxy]-2-methylindolizin-3-yl}methanone,
- 4-({[3-(4-amino-3-methoxybenzoyl)-2-methylindolizin-1-yl]oxy}methyl)benzoic acid,

- 3-(4-carboxybenzoyl)-2-methylindolizin-1-yl carboxylic acid,
- methyl 3-[(1-methoxy-2-methylindolizin-3-yl)carbonyl]benzoate,
- 4-[(1-methoxy-2-methylindolizin-3-yl)carbonyl]benzoic acid,
- 2-amino-5-[(1-methoxy-2-methylindolizin-3-yl)carbonyl]benzoic acid,
- 2-amino-5-({1-[(3-methoxybenzoyl)amino]-2-methylindolizin-3-yl}carbonyl)benzoic acid,
- 2-amino-5-({2-methyl-1-[(3,4,5-trimethoxybenzoyl)amino]indolizin-3-yl}carbonyl)benzoic acid, and
- 2-amino-5-({1-[(3-methoxyphenyl)sulphonyl]amino}-2-methylindolizin-3-yl}carbonyl)benzoic acid

or a pharmaceutically acceptable salt thereof.

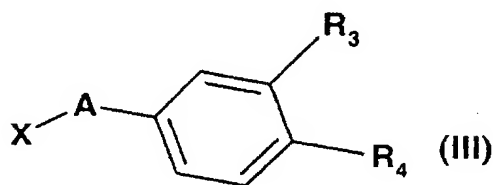
5. (Previously presented) A method for preparing the compounds according to Claim 1 wherein

A) an indolizine derivative of formula II,

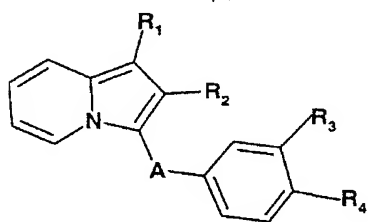


in which R<sub>1</sub> and R<sub>2</sub> have the meaning given for formula I, but R<sub>2</sub> does not represent a hydrogen atom or a haloalkyl radical,

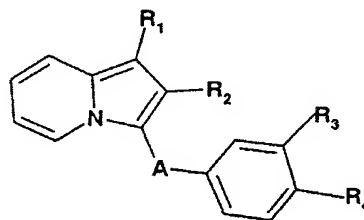
is condensed with a derivative of formula III,



in which X represents a halogen atom and  $R_3$  or  $R_4$ , which are identical or different, each represent a hydrogen atom, a nitro radical, a trifluoroacetamido radical or an alkoxy carbonyl radical of 2 to 6 carbon atoms, in order to obtain the compounds of formula Ia, Id or Ik,



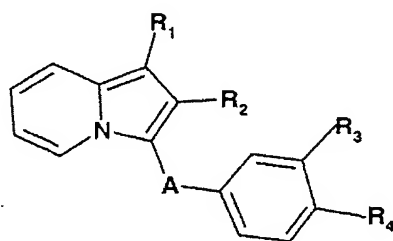
(Ia)



(Id)

$R_3$  and/or  $R_4 = \text{NO}_2$

$R_3$  and/or  $R_4 = -\text{CO}_2\text{Alkyl}$

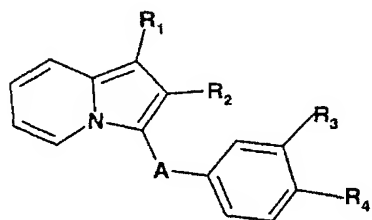


(Ik)

$R_3$  and/or  $R_4 = -\text{NH}-\text{COCF}_3$

and then,

- a) the compounds of formula Ia are subjected to a reduction in order to obtain the compounds of formula Ib,



(Ib)

$R_3$  and/or  $R_4 = -\text{NH}_2$



in which  $R_3$  and/or  $R_4$  represent an amino radical, which compounds of formula Ib then

- are subjected to the action of an alkyl halide in order to obtain the compounds of formula I in which  $R_4$  and/or  $R_3$  represent a radical  $-NR_5R_6$  (in which  $R_5$  represents a hydrogen atom and  $R_6$  represents an alkyl radical of 1 to 5 carbon atoms) and a radical  $-NH-Alk-NR_5R_6$  or a radical  $-NH-Alk-COOR_7$  (in which  $R_7$  does not represent a hydrogen atom) from which, by a subsequent saponification, the compounds of formula I are obtained in which  $R_4$  and/or  $R_3$  represent a radical  $-NH-Alk-COOR_7$  in which  $R_7$  represents a hydrogen atom,

or

- are subjected to acylation in order to obtain the compounds of formula I in which  $R_4$  and/or  $R_3$  represent a radical  $-NH-CO-Alk$ , or a radical  $-NH-CO-Alk-NR_9R_{10}$ , which are then subjected to alkylation in order to obtain a radical  $-N(R_{11})-CO-Alk$  or a radical  $-N(R_{11})-CO-Alk-NR_9R_{10}$  where  $R_{11}$  represents a radical  $-Alk-COOR_{12}$  in which  $R_{12}$  does not represent a hydrogen atom, the latter compounds are then optionally subjected to saponification in order to obtain the compounds of formula I in which  $R_4$  and/or  $R_3$  represent a radical  $-N(R_{11})-CO-Alk$  or a radical  $-N(R_{11})-CO-Alk-NR_9R_{10}$  where  $R_{11}$  represents a radical  $-Alk-COOH$ ,

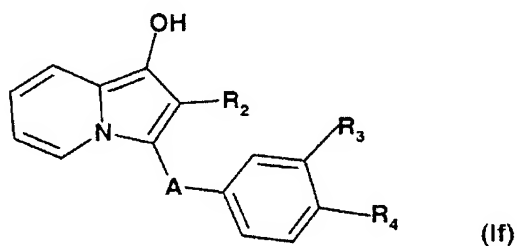
or

- are subjected to sulphonylation in order to obtain the compounds of formula I in which  $R_4$  and/or  $R_3$  represent a radical  $-NH-SO_2-Alk$  or a radical  $-NH-SO_2-Alk-NR_9R_{10}$ , which are then subjected to alkylation in order to obtain a radical  $-N(R_{11})-SO_2-Alk$  or a radical  $-N(R_{11})-SO_2-Alk-NR_9R_{10}$  where  $R_{11}$  represents a radical  $-Alk-COOR_{12}$  in which  $R_{12}$  does not represent a hydrogen atom, the latter compounds are then optionally subjected to saponification in order to obtain the compounds of formula I in which  $R_4$  and/or  $R_3$  represent a radical  $-N(R_{11})-SO_2-Alk$  or a radical  $-N(R_{11})-SO_2-Alk-NR_9R_{10}$  where  $R_{11}$  represents a radical  $-Alk-COOH$

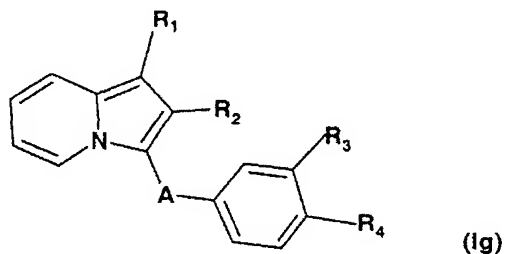
b) the compounds of formula Id in which  $R_3$  and/or  $R_4$  represent an alkoxy carbonyl radical are subjected to saponification in order to obtain the compounds of formula I in which  $R_3$  and/or  $R_4$  represent a carboxyl radical,

or

c) when  $R_1$  represents a benzyloxy radical, the compounds of formula Ia are subjected to the action of trifluoroacetic acid or the compounds of formula Id to hydrogenation, in order to obtain the compounds of formula If,



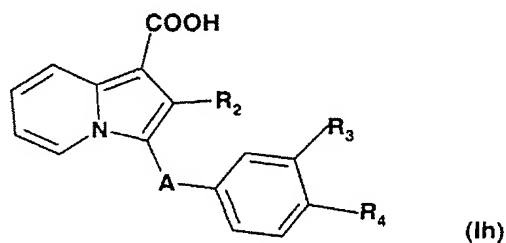
and then the compounds of formula If are subjected to O-alkylation in order to obtain the compounds of formula Ig,



in which  $R_3$  and/or  $R_4$  have the meanings given above, and  $R_1$  represents a linear or branched alkoxy radical of 1 to 5 carbon atoms, a radical  $-O-(CH_2)_n-cAlk$ , a radical  $-O-Alk-COOR_7$ , a radical  $-O-Alk-NR_5R_6$ , a radical  $-O-(CH_2)_n-Ph$ , or a radical  $-O-Alk-O-R_8$  – which, when  $R_8$  represents a radical  $-COCH_3$ , can give, by subsequent saponification, a radical  $-O-Alk-OH$  –, or a radical  $-O-Alk-CN$  which, by treatment with hydroxylamine, gives a radical  $-O-Alk-C(NH_2)=NOH$ ,

or

d) when  $R_1$  represents an alkoxycarbonyl radical, the compounds of formula Ia are subjected to saponification in order to obtain the compounds of formula Ih,

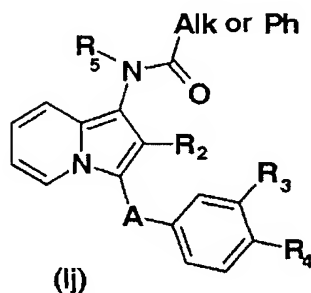
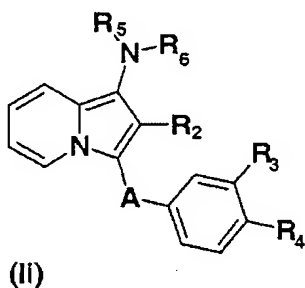


which are then subjected to the action of an amine derivative in order to obtain the compounds of formula I in which  $R_1$  represents a radical  $-CO-NH-Alk$ , or to the action of an amino acid derivative in order to obtain the compounds of formula I in which  $R_1$  represents a radical  $-CO-NH-(CH_2)_m-COOR_7$

or

e) when  $R_1$  represents a radical  $-NH-CO_2tButyl$ , the compounds of formula Ia or Id are subjected

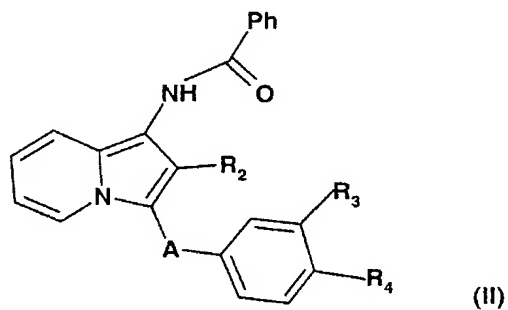
- either to alkylation followed by deprotection and an optional second alkylation in order to obtain the compounds of formula Ii,
- or to deprotection, followed by acylation in order to obtain the compounds of formula Ij in which  $R_5$  represents a hydrogen atom, followed by an optional alkylation in order to obtain the compounds of formula Ij in which  $R_5$  represents an alkyl radical



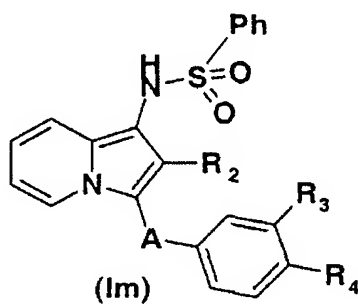
or

f) when  $R_1$  represents a radical  $-NH-CO_2t\text{Butyl}$ , the compounds of formula **Ik** are subjected

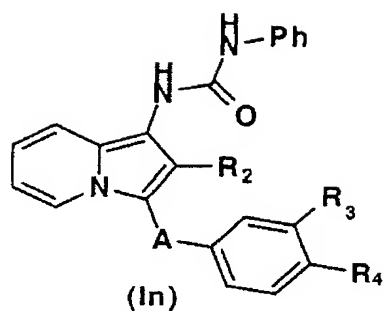
- either to deprotection, followed by acylation in order to obtain the compounds of formula II



- or to deprotection followed by sulfonylation in order to obtain the compounds of formula Im

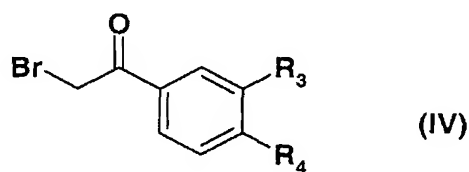


- or to deprotection, followed by a treatment with a phenyl isocyanate in order to obtain the compounds of formula In

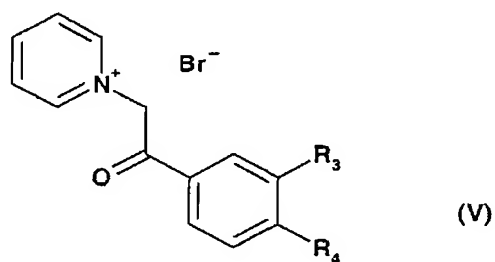


OR

**B)** when  $R_1$  represents an electron-attracting group,  $R_2$  represents a hydrogen atom or a haloalkyl radical and A represents a radical  $-CO-$ , pyridine is reacted with a bromoacetophenone of formula IV,



in order to obtain the compounds of formula V,



which are then subjected to a 1,3-dipolar cycloaddition with ethyl acrylate or a halogenated derivative of ethyl crotonate in the presence of an oxidizing agent in order to obtain the

compounds of formula Ia in which  $R_1$  represents an ethoxycarbonyl radical and  $R_2$  represents a hydrogen atom or a haloalkyl radical.

6 to 12. (Cancelled)

13. (Currently amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound according to Claim 1 together with a pharmaceutically acceptable excipient.

14. (Currently amended) A pharmaceutical composition comprising a therapeutically effective amount of a compound according to Claim 4 together with a pharmaceutically acceptable excipient.

15 to 30. (Cancelled)